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Edward Rebar

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EXAMINER

DUNSTON, JENNIFER ANN

ART UNIT

PAPER NUMBER

1636

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DELIVERY MODE

04/27/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/055,711	Applicant(s) REBAR ET AL.	
	Examiner JENNIFER DUNSTON	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,23-28,30-48 and 52-57 is/are pending in the application.
- 4a) Of the above claim(s) 1,23,24,33-35,38,42-48 and 52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-28,30-32,36,37,39-41 and 53-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1636

DETAILED ACTION

This action is in response to the amendment, filed 2/10/2009, in which claims 30 and 56 were amended. Claims 1, 23-28, 30-48 and 52-57 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group II (drawn to nucleic acid), species: DNA target sequence, zinc finger component comprising X(3)-Cys-X(2)-Cys-X(12)-His-X(3)-Z-X(4), target located in a plant cell, and a maize C1 activation domain in the replies filed on 8/3/2004 and 11/18/2004. This restriction requirement was made FINAL in the Office action mailed 2/9/2005 and reiterated in the Office action mailed 11/15/2005.

The requirement for the election of a specific zinc finger component, as set forth on pages 3-4 of the Office action mailed 7/1/2004 was withdrawn in the Office action mailed 6/14/2006. The remainder of the species election requirement was maintained in the Office action mailed 6/14/2006. Thus, the species election requirements for target sequence type (DNA), where the target is located (plant cell), and functional domain type (C1 activation domain) are maintained.

Claims 1, 33, 42-48 and 52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on 8/3/2004 and 11/18/2004.

Claims 23-24, 34-35 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on 8/3/2004 and 11/18/2004.

Currently, claims 25-28, 30-32, 36-37, 39-41 and 53-57 are under consideration.

Response to Arguments - Claim Objections

The objections of claims 25-28, 30-32, 36-37, 39-41 and 53-57 has been withdrawn in view of Applicant's amendment of claims 30 and 56 in the reply filed 2/10/2009.

Response to Arguments - 35 USC § 102

The rejection of claims 25-28, 30-32, 36-37, 39-41 and 53-56 under 35 U.S.C. 102(e) as being anticipated by Barbas, III et al (US Patent No. 7,151,201 B2) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. Barbas, III et al do not specifically teach 2, 3 or 4 amino acids between the two amino-terminal zinc coordinating residues and 1, 2, 3, 4, 6 or 7 amino acids between the carboxy-terminal zinc coordinating residues of the non-canonical zinc finger.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

Art Unit: 1636

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-28, 30-32, 36-37, 39-41, 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 7,151,201 B2, cited in a prior action; see the entire reference) in view of Filippova et al (Molecular and Cellular Biology, Vol. 16, No. 6, pages 2802-2813, June 1996; see the entire reference). This is a new rejection, necessitated by the amendment of claims 30 and 56 in the reply filed 2/10/2009.

Barbas, III et al teach nucleic acid molecules encoding zinc finger proteins that bind to a target nucleotide sequence of 3, 6, 9, 12, 15 or 18 nucleotides, where the zinc finger protein binds the target nucleotide sequence of the formula $(GNN)_n$, where N is any one of A, T, C or G and n is an integer from 1 to 6 (e.g., column 3, lines 13-43; column 18, lines 48-64; column 19, lines 53-57; Table 2). The region of the zinc finger protein that mediates the specific binding spans positions -1 to +6 of the alpha helix and, thus, is a recognition helix of seven amino acids in length (e.g., column 21, lines 34-39; boxed sequences in Figure 6). Barbas, III et al teach that any naturally occurring zinc finger protein can be used as a framework (or backbone) to derive a non-naturally occurring zinc finger with DNA binding specificity determined by alterations in

Art Unit: 1636

the alpha helix using known design rules (e.g., column 10, lines 55-67; column 11, lines 14-35; column 19, lines 28-34 and 53-57; column 21, lines 8-39; column 22, line 51 to column 25, line 9). Barbas, III et al teach that the target nucleotide sequence can be present in a plant cell and can be a promoter sequence (e.g., column 3, lines 23-50). Further, Barbas III et al teach that the target nucleotide sequence can be endogenous or exogenous to the target gene (e.g., column 3, lines 23-50). Barbas, III et al teach that the encoded zinc finger protein also includes an activation domain of a regulatory protein, such as a C1 activator domain of maize, in order to activate expression of the target gene operably linked to the target nucleotide sequence (e.g., column 4, lines 42-48; column 25, lines 10-46). Barbas, III et al teach expression vectors comprising the polynucleotide sequences encoding the zinc finger proteins, and plant host cells comprising the vectors (e.g., column 32, lines 10-36). Barbas, III et al teach the suspension of the polynucleotides in a pharmaceutically acceptable excipient that is an electroporation buffer of 0.3 M mannitol, 5 mM MES, 70 mM KCl, pH 5.8 (e.g., column 55, lines 35-67).

Barbas, III et al do not teach the isolated polynucleotide, where the polynucleotide encodes a non-canonical zinc finger component comprising a beta turn comprising two amino-terminal zinc coordinating cysteine residues separated by two amino acids and an alpha helix comprising one carboxy-terminal zinc coordinating histidine residue and one carboxy-terminal cysteine residue, where the carboxy-terminal histidine residue is amino terminal to the carboxy-terminal cysteine residue and the histidine and cysteine residues are separated by three amino acids.

Filippova et al teach nucleic acid molecules encoding the 11 zinc fingers of CTCF protein (e.g., page 2803, Isolation of human CTCF cDNAs; Figure 2A). Filippova et al teach that the

Art Unit: 1636

encoded CTCF protein binds DNA, and finger 11 is absolutely required for binding to the P2-proximal site A of human *c-myc* (e.g., page 2807, Different combinations of CTCF Zn fingers bind to divergent sequences in the chicken and human *c-myc* promoters; Figure 7C). Finger 11 of the CTCF DNA-binding protein contains the amino acid sequence **CSKCGKTFTRRNTMARHADNC** (e.g., Figure 2A). Thus, zinc finger 11 is a non-canonical zinc finger that contains two amino acids between the two amino-terminal zinc coordinating cysteine residues, and three amino acids between the two carboxy-terminal zinc coordinating residues. The two carboxy-terminal zinc coordinating residues consist of a histidine residue that is amino terminal to a cysteine residue.

Because Barbas, III et al disclose nucleic acid molecules encoding a zinc finger protein comprising a zinc finger domain from any naturally occurring protein that has been used as a framework for modifying the DNA binding specificity according to known design rules, and Filippova et al teach a nucleic acid molecule encoding a zinc finger protein that binds DNA, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the framework sequence encoding finger 11 (i.e., the CCHC zinc finger) of the CTCF protein of Filippova et al in the nucleic acid molecules of Barbas, III et al, where the finger 11 sequence has been modified to include a recognition helix that is engineered to bind the a target nucleic acid sequence taught by Barbas, III et al, to achieve the predictable result of making a polynucleotide that encodes a zinc finger polypeptide that binds to a plant promoter sequence containing the target nucleic acid sequence of Barbas, III et al. With respect to claims 28 and 54, which require the non-canonical zinc finger component to be the third zinc finger component or the first zinc finger component, respectively, it would have been obvious to one of ordinary skill

Art Unit: 1636

in the art at the time the invention was made to combine the zinc finger so Barbas III et al and Filippova et al in an order from N-terminus to C-terminus such that the non-canonical zinc fingers are present at the first and/or third zinc fingers. However, it is noted that the claims do not explicitly impose a linear order to the first, second and third zinc fingers.

Furthermore, one would have been motivated to include the sequence encoding the CCHC type zinc fingers of finger 11 of Filippova et al in order to expand the repertoire of available zinc finger nucleotide-binding proteins encoded by the polynucleotides. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 25-28, 30-32, 36, 39-41 and 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 7,329,728 B1; see the entire reference) in view of Filippova et al (Molecular and Cellular Biology, Vol. 16, No. 6, pages 2802-2813, June 1996; see the entire reference). This is a new rejection, necessitated by the amendment of claims 30 and 56 in the reply filed 2/10/2009.

Barbas, III et al teach nucleic acid molecules encoding fusion proteins, expression vectors containing the nucleic acids, and cells containing the expression vectors, where the cells are plant cells (e.g., column 2, lines 18-24; column 3, lines 12-14). Further, Barbas, III et al teach compositions comprising the nucleic acid molecule and a pharmaceutically acceptable excipient (e.g., column 5, lines 49-56). Barbas, III et al teach that the fusion protein encoded by the nucleic acid molecule includes at least one DNA binding domain, at least one ligand binding

Art Unit: 1636

domain, and at least one transcription modulating domain, and regulates expression by binding to a target sequence in a promoter (e.g., column 2, lines 59-67; column 5, line 66 to column 6, line 22; column 9, lines 56-60; column 17, lines 41-50; paragraph bridging columns 17-18). The transcription modulating domain may be a transcription activation domain (e.g., column 29, lines 30-34). In a preferred embodiment, the DNA binding domain includes at least three zinc finger modular units and binds to at least nine nucleotides (e.g., paragraph bridging columns 2-3; column 3, lines 59-64; paragraph bridging columns 20-21). For example, six zinc fingers will bind to a sequence of 18-bp (e.g., paragraph bridging columns 20-21). Barbas, III et al teach that it is advantageous to use zinc fingers, because of the ability to construct zinc fingers with unique specificity, which permits targeting and ligand-dependent control of expression of specific endogenous genes or exogenously administered genes (e.g., column 19, lines 28-35). Barbas, III et al teach that rules for creating synthetic zinc fingers with specificity to any desired target sequence are known (e.g., column 19, lines 36-49). Barbas, III et al teach that a zinc finger-nucleotide binding peptide domain contains a unique heptamer within the alpha-helical domain of the polypeptide, which heptameric sequence determines the binding specificity to the target nucleotide (e.g., column 20, lines 43-53). Further, Barbas, III et al teach that any framework sequences known in the art to function as part of a zinc finger protein can be modified to include a peptide nucleotide-binding domain (e.g., column 20, line 43 to column 21, line 20).

Barbas, III et al do not teach the isolated polynucleotide, where the polynucleotide encodes a non-canonical zinc finger component comprising a beta turn comprising two amino-terminal zinc coordinating cysteine residues separated by two amino acids and an alpha helix comprising one carboxy-terminal zinc coordinating histidine residue and one carboxy-terminal

Art Unit: 1636

cysteine residue, where the carboxy-terminal histidine residue is amino terminal to the carboxy-terminal cysteine residue and the histidine and cysteine residues are separated by three amino acids.

Filippova et al teach nucleic acid molecules encoding the 11 zinc fingers of CTCF protein (e.g., page 2803, Isolation of human CTCF cDNAs; Figure 2A). Philippova et al teach that the encoded CTCF protein binds DNA, and finger 11 is absolutely required for binding to the P2-proximal site A of human *c-myc* (e.g., page 2807, Different combinations of CTCF Zn fingers bind to divergent sequences in the chicken and human *c-myc* promoters; Figure 7C). Finger 11 of the CTCF DNA-binding protein contains the amino acid sequence **CSKCGKTFTRRNTMARHADNC** (e.g., Figure 2A). Thus, zinc finger 11 is a non-canonical zinc finger that contains two amino acids between the two amino-terminal zinc coordinating cysteine residues, and three amino acids between the two carboxy-terminal zinc coordinating residues. The two carboxy-terminal zinc coordinating residues consist of a histidine residue that is amino terminal to a cysteine residue.

Because Barbas, III et al disclose nucleic acid molecules encoding a zinc finger protein comprising a zinc finger domain from any naturally occurring protein that has been used as a framework for modifying the DNA binding specificity according to known design rules, and Philippova et al teach a nucleic acid molecule encoding a zinc finger protein that binds DNA, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the framework sequence encoding finger 11 (i.e., the CCHC zinc finger) of the CTCF protein of Philippova et al in the nucleic acid molecules of Barbas, III et al, where the finger 11 sequence has been modified to include a recognition helix that is engineered to bind the a target

Art Unit: 1636

nucleic acid sequence taught by Barbas, III et al, to achieve the predictable result of making a polynucleotide that encodes a zinc finger polypeptide that binds to a plant promoter sequence containing the target nucleic acid sequence of Barbas, III et al. With respect to claims 28 and 54, which require the non-canonical zinc finger component to be the third zinc finger component or the first zinc finger component, respectively, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the zinc finger so Barbas III et al and Filippova et al in an order from N-terminus to C-terminus such that the non-canonical zinc fingers are present at the first and/or third zinc fingers. However, it is noted that the claims do not explicitly impose a linear order to the first, second and third zinc fingers.

Furthermore, one would have been motivated to include the sequence encoding the CCHC type zinc fingers of finger 11 of Filippova et al in order to expand the repertoire of available zinc finger nucleotide-binding proteins encoded by the polynucleotides. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 7,329,728 B1; see the entire reference) in view of Filippova et al (Molecular and Cellular Biology, Vol. 16, No. 6, pages 2802-2813, June 1996; see the entire reference) as applied to claims 25-28, 30-32, 36, 39-41 and 53-57 above, and further in view of Guyer et al (Genetics, Vol. 149, pages 633-639, 1998, cited in a prior action; see the entire reference). This

Art Unit: 1636

is a new rejection, necessitated by the amendment of claims 30 and 56 in the reply filed 2/10/2009.

The combined teachings of Barbas, III et al and Filippova et al are described above and applied as before.

Barbas, III et al and Filippova et al do not teach the polynucleotide where the activation domain is a maize C1 activation domain.

Guyer et al teach *Arabidopsis* plants comprising a stably integrated hybrid transcription factor, and plants comprising an activatable transgene, where the hybrid transcription factor and activatable transgene are brought together in the same cell by fertilization (e.g. paragraph bridging pages 633-634). Specifically, Guyer et al teach a GAL4 DNA binding domain fused to a maize C1 transcription activation domain as the hybrid transcription factor, and a reporter transgene controlled by a synthetic promoter comprising ten GAL4 DNA binding sites (e.g. paragraph bridging pages 633-634; Figure 1). Further, Guyer et al teach that many positive transcriptional regulatory factors are modular, consisting of a DNA-binding domain and an activation domain and that fusing combinations of these elements derived from different kingdoms results in the production of diverse hybrid factors having defined DNA-binding specificity and transcriptional activation function with advantages over expression under direct control by a natural promoter (e.g. page 633, left column; page 638, paragraph bridging columns).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the polynucleotide to comprise a C1 activation domain taught by Guyer et al because Barbas, III et al teach it is within the skill of the art to make a plant cell comprising the

Art Unit: 1636

polynucleotide where the polynucleotide encodes a zinc finger-nucleotide binding polypeptide that activates expression of a gene operably linked to the target nucleotide sequence, and Guyer et al teach that the maize C1 activation domain functions in a plant cell to activate transcription from a heterologous DNA binding domain.

One would have been motivated to specifically use the maize C1 activation domain, because it was known in the art to function in plants. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 25-28, 30-32, 36-37, 39-41 and 53-57 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 7,151,201 B2) in view of Jiang et al (The Journal of Biological Chemistry, Vol. 271, No. 18, pages 10723-10730, 1996) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The references do not specifically teach 2, 3 or 4 amino acids between the two amino-terminal zinc coordinating residues and 1, 2, 3, 4, 6 or 7 amino acids between the carboxy-terminal zinc coordinating residues of the non-canonical zinc finger.

The rejection of claims 25-28, 30-32, 36, 39-41 and 53-57 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 6,242,568) in view of Jiang et al (The Journal of Biological Chemistry, Vol. 271, No. 18, pages 10723-10730, 1996) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The

Art Unit: 1636

references do not specifically teach 2, 3 or 4 amino acids between the two amino-terminal zinc coordinating residues and 1, 2, 3, 4, 6 or 7 amino acids between the carboxy-terminal zinc coordinating residues of the non-canonical zinc finger.

The rejection of claim 37 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 6,242,568) in view of Jiang et al (The Journal of Biological Chemistry, Vol. 271, No. 18, pages 10723-10730, 1996), and further in view of Guyer et al (Genetics, Vol. 149, pages 633-639, 1998) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The references do not specifically teach 2, 3 or 4 amino acids between the two amino-terminal zinc coordinating residues and 1, 2, 3, 4, 6 or 7 amino acids between the carboxy-terminal zinc coordinating residues of the non-canonical zinc finger.

The rejection of claims 25-28, 30-32, 36, 39-41 and 53-55 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 6,242,568) in view of Hori et al (J. Am. Chem. Soc. Vol. 122, pages 7648-7653, July 29, 2000) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The references do not teach the claimed non-canonical zinc finger component.

The rejection of claim 37 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 6,242,568) in view of Hori et al (J. Am. Chem. Soc. Vol. 122, pages 7648-7653, July 29, 2000), and further in view of Guyer et al (Genetics, Vol. 149, pages 633-639, 1998) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The references do not teach the claimed non-canonical zinc finger component.

The rejection of claims 56 and 57 under 35 U.S.C. 103(a) as being unpatentable over Barbas, III et al (US Patent No. 6,242,568) in view of Hori et al (J. Am. Chem. Soc. Vol. 122,

Art Unit: 1636

pages 7648-7653, July 29, 2000), and further in view of Jiang et al (The Journal of Biological Chemistry, Vol. 271, No. 18, pages 10723-10730, 1996) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/10/2009. The references do not teach the claimed non-canonical zinc finger component.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

Art Unit: 1636

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Celine X Qian /
Primary Examiner, Art Unit 1636